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The efficacy and safety of tranexamic acid in transforaminal lumbar interbody fusion: a systematic review and meta-analysis

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- *Purpose:* This meta-analysis aimed to assess the efficacy and safety of tranexamic acid (TXA) in transforaminal lumbar interbody fusion (TLIF), focusing on its impact on intraoperative blood loss and related outcomes.
- *Methods:* The review process was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. We searched the PubMed, EMBASE, Medline, and Cochrane Library databases to identify all literature related with TXA and TLIF. Finally, five trials ultimately meeting the inclusion criteria. Continuous variables were analyzed using mean difference and categorical variables were analyzed using Peto odds ratio, via random effects models.
- *Results:* The meta-analysis revealed a significant reduction in intraoperative blood loss associated with TXA use during TLIF, as confirmed by the RCTs. However, the impact of TXA on other outcomes, such as postoperative drainage volume, total blood loss, and length of hospital stay, remains inconclusive due to limited data. No severe complications related to TXA use were reported, providing preliminary evidence of its safety in TLIF.
- *Conclusion:* TXA appears to effectively reduce intraoperative blood loss in TLIF, based on the available RCT evidence. However, further research is needed to provide a comprehensive assessment of TXA's overall impact on various outcomes in this context. This meta-analysis underscores the importance of ongoing investigation to establish the full potential and safety profile of TXA in TLIF procedures.

Keywords

- tranexamic acid
- transforaminal lumbar interbody fusion
- intraoperative blood loss
- meta-analysis

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Background

Transforaminal lumbar interbody fusion (TLIF) is a surgical method widely used to treat spinal diseases such as herniated discs, lumbar spondylolisthesis, and lumbar stenosis (1, 2, 3). With the rapid development of aging society and the influence of modern lifestyles, the incidence of these spinal diseases is gradually increasing. However, the hematopoietic function and surgery tolerance of the elderly are poor, and the muscles and surrounding tissues need to be peeled off during the operation, and the wound bleeding is more (4). High blood loss not only increases the patient's need for blood transfusion and prolongs the operation time but can also lead to various postoperative complications such as infection, delayed healing, prolonged hospital stay, and increased medical costs (5). Therefore, how to effectively reduce bleeding during surgery has become the focus of many spine surgeons and researchers. Commonly used methods include the use of hemostatic drugs and autologous blood transfusion devices, as well as surgical modifications to reduce soft tissue damage. Tranexamic acid (TXA), as a synthetic antifibrinolytic drug, has been shown to significantly reduce bleeding during surgery in many surgical procedures. Its mechanism of action is to reduce bleeding by inhibiting the production and activity of plasmin, thereby preventing the dissolution of fibrin.

Previous meta-analyses have evaluated the safety and efficacy of tranexamic acid in spinal surgery. Based on a meta-analysis of 20 RCTs, Liu *et al.* demonstrated that TXA reduces blood loss, reduces transfusion rates,

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shortens hospital stay, and does not increase the incidence of postoperative complications in open spine surgery (6). Qin *et al.*, in a meta-analysis of different doses of tranexamic acid, found that high-dose intravenous TXA reduced intraoperative blood loss (IBL), retained higher postoperative Hb and HCT levels, and did not increase surgical time and transfusion rates compared with low doses (7). Brown *et al.* conducted a meta-analysis of patients undergoing posterior spinal surgery and found that TXA significantly reduced blood loss from cervical, thoracic, and lumbar laminectomy and fusion surgery while showing minimal complications (8). Bai *et al.* conducted a meta-analysis evaluating risks in patients with posterior lumbar fusion and came to conclusions consistent with studies by other scholars (9). However, no meta-analysis of TLIF has been reported. TLIF is different from other lumbar fusion surgery, which is lumbar fusion through one side of the intervertebral foramen approach. Compared with traditional fusion surgery, there is less damage to soft tissues, less surgical trauma, and less IBL. Kanhere *et al.* found that intravenous tranexamic acid had no effect on IBL (10). However, other studies have found that preoperative tranexamic acid reduces IBL during TLIF (11, 12). In light of this, we decided to conduct this meta-analysis study to determine the specific effects of TXA in TLIF surgery and its potential effects. This is important to guide clinical practice and provide patients with safer and more effective treatment options.

Methods

This meta-analysis was performed in agreement with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. The protocol for this meta-analysis was registered on PROSPERO (Registration No: CRD 42023459675).

Inclusion criteria

Study type: randomized controlled trial or cohort study or case–control study. Study population: patients undergoing TLIF. Intervention and control: TXA in the treatment group and no TXA in the control group. Outcome index: intraoperative blood loss, total drain volume, total blood loss, hospital stay after surgery, postoperative hemoglobin 1 day after surgery, and complication.

Exclusion criteria

Letters, case reports, meeting, reviews, animal trials, or republished studies; unused TXA in the treatment group; studies lacking a control group; patients with a past medical history of coagulopathy, bleeding disorders, seizures, blood clots, cancer, or motor disease.

Outcomes

The primary outcome was the incidence of intraoperative blood loss. Secondary outcomes were the total drain volume, total blood loss, hospital stay after surgery, postoperative hemoglobin 1 day after surgery, and complication.

Search strategy

One of the authors performed the search in PubMed (Medline), EMBASE, Web of Science, and the Cochrane Central Register of Controlled Trials from the inception dates to September 01, 2023, using the keywords '(tranexamic acid or TXA) and (lumbar or spin*) and (transforaminal lumbar interbody fusion or TLIF)'. We also searched the ICTRP (International Clinical Trials Registry Platform) portal maintained by the World Health Organization to identify ongoing or unpublished eligible trials and the reference lists of articles retrieved from the electronic search for related articles. No language restrictions were applied during the search.

Study selection

Two researchers individually screened the retrieved literature strictly against inclusion and exclusion criteria. First, by reading the title and abstract, the documents that met the inclusion criteria were read in full and the included documents were finally confirmed. If the two researchers did not agree during the literature screening process, it was left to the senior researcher.

Data collection process

Data on relevant outcome measures were extracted from the literature that met the inclusion criteria, including author year, study design type, country, sample size, participants, TXA treatment, age, and outcomes.

Assessment of risk of bias and quality of evidence

Two researchers independently assessed the quality of all included trials based on Cochrane risk-of-bias criteria (13). The Newcastle–Ottawa scale (NOS) was used to evaluate the literature quality of the retrospective studies (14).

Data synthesis

The meta-analysis was performed using Stata (version 17; StataCorp, 2021) software. The heterogeneity was assessed by using the Q test and I^2 value calculation. The odds ratio (OR) and their associated 95% confidence interval (CI) were used to assess outcomes for dichotomous outcomes. Continuous outcomes were analyzed using mean, S.D., and sample size to provide a mean difference (MD) between the TXA and control

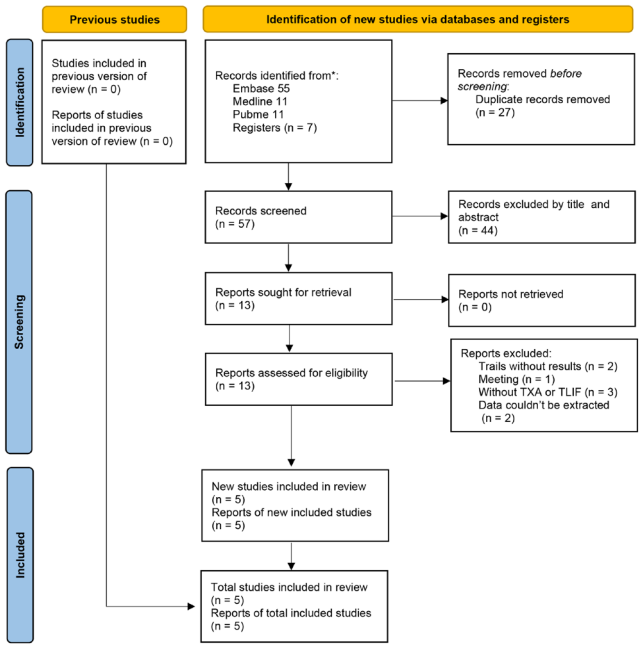

Figure 1
Flow diagram for search and selection of included studies.

groups. A *P*-value less than 0.05 suggested that the difference was statistically significant.

Sensitivity analysis

We performed a sensitivity analysis by excluding the largest trial; excluding cluster randomized or quasi randomized trials; excluding trials with high risk of bias; and by using random effect models.

Results

After a total of 84 studies were identified, 27 duplicates were removed and 44 irrelevant studies were excluded based on titles and abstracts. The full text of 13 articles were read and 8 articles were eliminated. These included one meeting (15), two registered studies without results (16, 17), one study performed on posterior lumbar interbody fusion (18), two studies that were unable to extract data from patients with TLIF (19, 20), one study that did not use tranexamic acid (21), and one study that compared oral tranexamic acid with intravenous use (22). Finally, five trials with three RCT studies and two retrospective studies, totaling 984 patients, were included in our study (10, 11, 12, 23, 24). The literature screening process is shown in Fig. 1. Three RCTs were at risk of bias with reference to the Cochrane Manual of Systematic Review of Interventions. The basic characteristics of the included studies are shown in Table 1.

Intraoperative blood loss

Five studies included IBL as the primary outcome (10, 11, 12, 23, 24). Three RCT studies and two retrospective studies were included (Table 2). The study by Zhang *et al.* included two treatment groups, and we combined the data from the two treatment groups according to the comments of the Cochrane Manual and performed statistical calculations (24). Due to significant heterogeneity in studies ($I^2 > 50\%$, $P < 0.1$), a random-effects model was used. The use of tranexamic acid significantly reduced IBL in RCT studies (MD: −68.91, 95% CI: −135.28 to −2.53, $I^2 = 85.7\%$, $P = 0.042$; Fig. 2). For retrospective studies, tranexamic acid was not statistically significant between the two groups in terms of IBL compared with control (MD: −157.83, 95% CI: −578.01−262.34, $I^2 = 98.4\%$, $P = 0.462$; Fig. 2).

Total drain volume

In total, two studies reported on postoperative drainage, including one RCT and one retrospective study (10, 11). Considering that they were of different types of studies, it was not possible to pool the results. There was no statistically significant difference between the two groups in the results reported by He *et al.* (11). However, Kanhere *et al.* found that tranexamic acid was able to retrieve postoperative drainage with a statistically significant difference (10).

Total blood loss

Only Kanhere *et al.* reported total blood loss, and they concluded that tranexamic acid could not reduce total blood loss (10).

Table 1 Characteristics of included studies.

Study	Country	Date range	Design	No. of subjects		Age (years)	
				TXA	Control	TXA	Control
He *et al.* (11)	China	July 2018–February 2019	RCT	20	20	57.95 ± 12.44	57.9 ± 11.76
Kanhere *et al.* (10)	USA	January 2017–July 2021	Cohort study	183	315	59.3 ± 11.7	61.4 ± 10.6
Mallepally *et al.* (23)	India	November 2017–October 2018	Case controlled	175	75	55.8 ± 13.0	55.3 ± 12.8
Wang *et al.* (12)	China	March 2014–December 2016	RCT	39	41	41.2 ± 10.3	42.5 ± 9.5
Zhang *et al.* (24)	China	September 2019–October 2020	RCT	39	38	56.95 ± 11.41; 55.67 ± 14.32	54.84 ± 10.62

RCT, randomized controlled trials; TXA, tranexamic acid.

Table 2 Risk of bias, TXA administration for the patients' condition, and reported outcomes in the included studies.

Study	Risk of bias*	Patients' condition	TXA administration	Outcomes
He *et al.* (11)	Low	Degenerative conditions	10 mg/kg i.v. before skin incision + 6–8 mg/kg/h i.v. during the surgery	IBL, total postoperative drainage, time for drainage removal, hospital stay after surgery, hematological parameters, blood transfusion, complication
Kanhere *et al.* (10)	NOS (8)	Degenerative conditions	10 mg/kg i.v. before skin incision	Length of stay, 90-day readmissions, estimated blood loss, pre- and postoperative hemoglobin, operative length, transfusion requirement, and drain output per day.
Mallepally *et al.* (23)	NOS (8)	Degenerative conditions	Wound soaked with TXA (1 g in 100 mL saline solution) for 3 min before wound closure	IBL, operative duration, drain volume, drainage on postoperative days 1 and 2, time for drain removal, hematological parameters
Wang *et al.* (12)	Low	Type C fracture–dislocation of the thoracolumbar junction (T11L2)	10 mg/kg i.v. before skin incision + 1 mg/kg/h during the surgery.	IBL, hematological parameters
Zhang *et al.* (24)	Unclear	Single level of degenerative conditions	20 or 50 mg/kg i.v. before skin incision	IBL, postoperative drainage, operative duration, total blood loss, hidden blood loss, transfusion requirement, hematological parameters, complication

*Risk of bias assessment tool (RCTs) or NOS (observational).
IBL, intraoperative blood loss; NOS, Newcastle–Ottawa Scale; TXA tranexamic acid.

Hospital stay after surgery

Three studies reported length of hospital stay after surgery, including one RCT study and two retrospective studies (10, 11, 23). A meta-analysis of two retrospective studies found that tranexamic acid did not reduce the length of hospital stay after surgery (Fig. 3). The RCT results of He *et al.* showed that tranexamic acid compared to the control group shortened the postoperative hospital stay of patients.

Postoperative hemoglobin 1 day after surgery

A total of two studies (one RCT and one non-RCT) reported postoperative hemoglobin 1 day after surgery (10, 11). Both studies indicated no difference between the two groups.

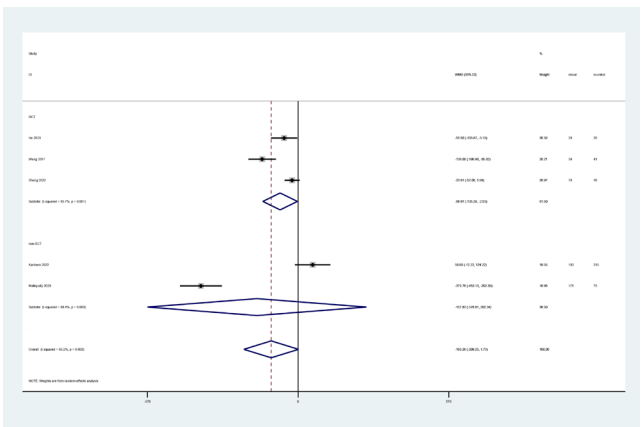

Figure 2
Forest plot of comparison: TXA vs no TXA; outcome: intraoperative blood loss.

Complications

A total of three studies reported complications (11, 12, 24). Among them, He *et al.* reported nine cases of postoperative occurrence, but these complications were related to incision infection and hypoproteinemia, and none of them occurred with complications such as vascular embolism.

Sensitivity analysis

The remaining studies were combined when any individual study was excluded. No individual study had a significant impact on the results.

Risk of bias

As fewer than ten trials were included, no publication bias assessment was performed by funnel plots.

Discussion

In our meta-analysis, we systematically assessed the efficacy and safety of tranexamic acid in TLIF surgery. Results from randomized controlled trials have shown that tranexamic acid significantly reduces intraoperative blood loss. However, this effect was not observed in retrospective studies, possibly due to its inherent selection and information bias, resulting in results confounded by other unadjusted variables. Among retrospective studies, Mallepally *et al.* discussed the effect of topical tranexamic acid on intraoperative blood loss (23). They soaked the incision with tranexamic acid solution for 3 min before surgically closing it, and then sutured the incision. Although final topical soaking with TXA solution may also reduce intraoperative bleeding, it is more likely to reduce postoperative drainage. Hui *et al.* conducted a meta-

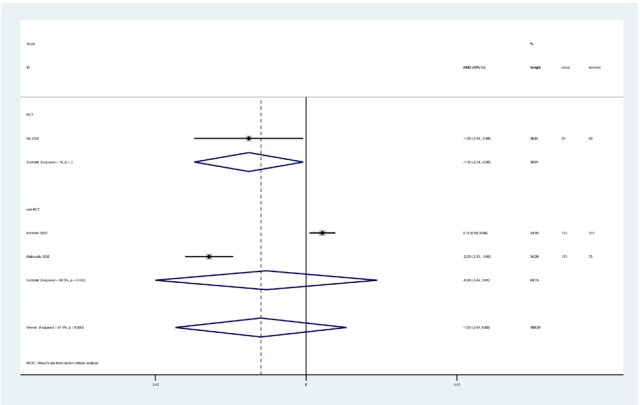

Figure 3
Forest plot of comparison: TXA vs no TXA; outcome: hospital stay after surgery.

analysis of topical TXA and found that it significantly reduced the occurrence of postoperative drainage, and the included studies rarely reported intraoperative blood loss (25). Therefore, we prefer to base the results of randomized controlled trials. With regard to total drain volume, although a limited number of studies have been conducted, there is evidence that TXA may help reduce total drain volume (11). This is also consistent with its pharmacological action. On the other hand, the Kanhere *et al.* study suggests that TXA does not affect total blood loss (10), which may mean that its benefits in TLIF surgery may be somewhat limited or related to the specific environment and patient characteristics of the study. Or because we included fewer studies, we were unable to pool results and could only perform descriptive analyses of previous studies. In addition, there were discrepancies in data on length of hospital stay after surgery. Although some studies have shown that TXA may shorten the length of hospital stay in patients, this is not a universal observation, suggesting that the length of hospital stay after surgery may be more influenced by other factors such as the patient's general health and surgical complications. To date, no serious complications associated with tranexamic acid use have been identified, providing preliminary evidence of its safety in TLIF. However, further studies in larger patient populations are needed to draw more convincing conclusions.

As an antifibrinolytic hemostatic agent, TXA blocks plasmin from binding to fibrin by binding to the lysine site of plasminogen, and it can also inhibit fibrinolysis to achieve hemostasis. At present, it is widely used in surgery with large blood loss such as joint replacement and spinal fusion, which can significantly reduce the amount of blood loss and transfusion rate during the perioperative period (26). With its wide application, its safety and effectiveness in the process of use need to be further explored.

Based on the available researches evidence, the effectiveness of TXA in spinal surgery (including reducing blood loss, lowering hemoglobin, and reducing the incidence of blood transfusion) has been recognized (6, 27, 28). For the safety of its use, there is a theoretical risk of increased thrombotic events, including deep vein thrombosis, pulmonary embolism, myocardial infarction, and ischemic cerebral infarction (29, 30). In our study, we also did not find that TXA use increased the occurrence of events such as blood clots. However, Luo *et al.* reported a case of persistent convulsions in both lower extremities after topical tranexamic acid. After analysis, it is considered that high concentrations of tranexamic acid entering the cerebrospinal fluid led to direct inhibition of γ-aminobutyric acid and glycine receptors in the posterior site of neurons in the dorsal horns of the spinal cord, thereby increasing excitability and leading to the development of persistent convulsions in patient (31). TLIF is prone to damage to the dura because it is performed next to the dura. Mallepally *et al.* compared studies of topical tranexamic acid in TLIF surgery, although no complications such as related seizures occurred (23). However, given the potentially lethal risk of tranexamic acid entering the spinal canal, we continue to urge patients with suspected dural rupture intraoperatively to avoid topical tranexamic acid intraoperatively.

Strengths and limitations

To our knowledge, this is the first study to estimate the efficacy and safety of tranexamic acid in TLIF surgery. This specific scope of research provides a valuable reference for specific patient populations and clinicians. This meta-analysis pooled five published studies involving 984 participants; this large overall sample size may improve the statistical power of the data analysis and thus provide more reliable estimates than the single studies. A clear advantage of this study is the in-depth comparison and analysis of RCTs separately from non-RCT studies. This approach ensures that the inherent differences between different types of studies are properly managed when assessing the effects of tranexamic acid in TLIF procedures, while effectively reducing the potential risk of bias. Through independent analysis of both types of studies, we enhanced our confidence in the conclusions, especially when both yielded similar results, providing readers with clearer and more convincing conclusions.

However, our study also had certain limitations. First, our meta-analysis included only five trials, of which three were RCTs and two were retrospective studies. Such a small sample size and variant study type may limit the statistical power and generalizability of the results. Second, heterogeneity (I^2) was high when analyzing

intraoperative blood loss. This high degree of heterogeneity suggests that there may be significant differences between studies, possibly due to different patient populations, surgical techniques, doses, or other unknown factors. Third, only one study reported total blood loss, and data on others, such as postoperative drainage, length of hospital stay, and hemoglobin levels at 1 day postoperatively, were relatively lacking, limiting the assessment of the full effect of tranexamic acid. Fourth, as fewer than ten included studies did not perform funnel assessments, this may have hidden the presence of publication bias. Fifth, there were differences in the dose of tranexamic acid used between the different included studies. This means that our analysis may be influenced by a variety of dosages and regimens, which may affect the consistency and interpretability of results. Sixth, different doses may result in different intensity of effects, which require special attention when interpreting the overall results, and given the small number of studies we included, subgroup analysis is not possible, and further research is expected in subsequent studies. Future studies or meta-analyses based on similar doses or regimens of use may yield more accurate and robust conclusions.

Conclusions

After a comprehensive analysis of multiple studies, we found that the use of tranexamic acid in TLIF showed significant effects in reducing intraoperative blood loss. However, the number of included studies for postoperative drainage, total blood loss, length of hospital stay, and other relevant outcomes is limited, and more studies are needed to more accurately assess the overall effect of tranexamic acid.

ICMJE Conflict of Interest
The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the study reported.

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Author contribution statement
HL conceived the study. XY developed the research protocol. XY and YR performed the literature search. WP and HZ screened titles and abstracts and reviewed full texts. YR and HL performed data abstraction. HL prepared the first manuscript draft. All authors contributed to final edits and revisions prior to submission.

References

1. Khalifeh JM, Massie LW, Dibble CF, Dorward IG, Macki M, Khandpur U, Alshohatee K, Jain D, Chang V & Ray WZ. Decompression of lumbar central spinal canal stenosis following minimally invasive transforaminal lumbar interbody fusion. *Clinical Spine Surgery* 2021 **34** E439–E449. (https://doi.org/10.1097/BSD.0000000000001192)

2. Steinhaus ME, Vaishnav AS, Shah SP, Clark NJ, Chaudhary CB, Othman YA, Urakawa H, Samuel AM, Lovecchio FC, Sheha ED, ***et al.*** Does loss of spondylolisthesis reduction impact clinical and radiographic outcomes after minimally invasive transforaminal lumbar interbody fusion? *Spine Journal* 2022 **22** 95–103. (https://doi.org/10.1016/j.spinee.2021.06.009)

3. Sun WX, Liu HN, Chen MT, Lin YP, Wang HS & Chen BL. Meta-analysis of the clinical efficacy and safety of oblique lateral interbody fusion and transforaminal interbody fusion in the treatment of degenerative lumbar spondylolisthesis. *EFORT Open Reviews* 2022 **7** 663–670. (https://doi.org/10.1530/EOR-22-0042)

4. Groarke EM & Young NS. Aging and hematopoiesis. *Clinics in Geriatric Medicine* 2019 **35** 285–293. (https://doi.org/10.1016/j.cger.2019.03.001)

5. Ross D, Erkocak O, Rasouli MR & Parvizi J. Operative time directly correlates with blood loss and need for blood transfusion in total joint arthroplasty. *Archives of Bone and Joint Surgery* 2019 **7** 229–234.

6. Liu ZG, Yang F, Zhu YH, Liu GC, Zhu QS & Zhang BY. Is tranexamic acid beneficial in open spine surgery? and its effects vary by dosage, age, sites, and locations: a meta-analysis of randomized controlled trials. *World Neurosurgery* 2022 **166** 141–152. (https://doi.org/10.1016/j.wneu.2022.07.044)

7. Qin C, Du KL, Guo PY, Gong HD & Zhang CQ. Tranexamic acid dosage for spinal surgery: a meta-analysis. *European Spine Journal* 2022 **31** 2493–2501. (https://doi.org/10.1007/s00586-022-07315-7)

8. Brown NJ, Choi EH, Gendreau JL, Ong V, Himstead A, Lien BV, Shahrestani S, Ransom SC, Tran K, Tafreshi AR, ***et al.*** Association of tranexamic acid with decreased blood loss in patients undergoing laminectomy and fusion with posterior instrumentation: a systematic review and meta-analysis. *Journal of Neurosurgery. Spine* 2022 **36** 686–693. (https://doi.org/10.3171/2021.7.SPINE202217)

9. Bai J, Zhang P, Liang Y, Wang J & Wang Y. Efficacy and safety of tranexamic acid usage in patients undergoing posterior lumbar fusion: a meta-analysis. *BMC Musculoskeletal Disorders* 2019 **20** 390. (https://doi.org/10.1186/s12891-019-2762-2)

10. Kanhere AP, Lambrechts MJ, Issa TZ, Karamian BA, Hendow CJ, Reddy YC, Slota PJ, D'Antonio ND, Kaye ID, Canseco JA, ***et al.*** The effect of tranexamic acid on operative and postoperative blood loss in transforaminal lumbar interbody fusions. *World Neurosurgery* 2022 **166** e443–e450. (https://doi.org/10.1016/j.wneu.2022.07.020)

11. He B, Li Y, Xu S, Ou Y & Zhao J. Tranexamic acid for blood loss after transforaminal posterior lumbar interbody fusion surgery: a double-blind, placebo-controlled, randomized study. *BioMed Research International* 2020 **2020** 8516504. (https://doi.org/10.1155/2020/8516504)

12. Wang W, Duan K, Ma M, Jiang Y, Liu T, Liu J & Hao D. Tranexamic acid decreases visible and hidden blood loss without affecting Prethrombotic State molecular markers in transforaminal thoracic interbody fusion for treatment of thoracolumbar fracture-dislocation. *Spine* 2018 **43** E734–E739-e9. (https://doi.org/10.1097/BRS.0000000000002491)

13. Cumpston M, Li T, Page MJ, Chandler J, Welch VA, Higgins JP & Thomas J. Updated guidance for trusted systematic reviews: a new edition of the Cochrane Handbook for Systematic Reviews of Interventions. *Cochrane Database of Systematic Reviews* 2019 **10** ED000142. (https://doi.org/10.1002/14651858.ED000142)

14. Wells G, Shea B & O'Connell J. *The Newcastle-Ottawa Scale (NOS) for Assessing the Quality of Nonrandomised Studies in Meta-analyses*. Ottawa Health Research Institute Web Site 2014. Available at: https://www.ohri.ca/programs/clinical_epidemiology/oxford.asp

15. Kanhere A, Lambrechts M, D'Antonio N, Reddy Y, Slota P, Canseco JA, Hilibrand AS, Kepler CK, Vaccaro AR & Schroeder GD. The effect of tranexamic acid on operative and postoperative blood loss in transforaminal lumbar interbody fusion. *Spine Journal* 2022 **22** S196–S197. (https://doi.org/10.1016/j.spinee.2022.06.402)

16. ChiCtr. *Feasibility Study of Tranexamic Acid on Reducing Perioperative Hidden Blood Loss during Transforaminal Lumbar Interbody Fusion* 2019. Available at: http://wwwwhoint/trialsearch/Trial2aspx?TrialID=ChiCTR1900027107

17. ChiCtr. *Tranexamic acid, Batroxobin and their Combination for spinal surgery* 2019. Available at: https://trialsearchwhoint/Trial2aspx?TrialID=ChiCTR1900024148

18. Arun-Kumar V & Naresh-Babu J. Is there a role for preoperative local infiltration of tranexamic acid in elective spine surgery? A prospective randomized controlled trial analyzing the efficacy of intravenous, local infiltration, and topical administration of tranexamic acid. *Global Spine Journal* 2021 **11** 21–27. (https://doi.org/10.1177/2192568219888446)

19. Li X, Jiao G, Li J, Ji W, Hao Z, Gong F & Chen Y. Combined use of tranexamic acid and Rivaroxaban in posterior/transforaminal lumbar interbody fusion surgeries safely reduces blood loss and incidence of thrombosis: evidence from a prospective, randomized, double-blind, placebo-controlled study. *Global Spine Journal* 2023 **13** 1229–1237. (https://doi.org/10.1177/21925682211024556)

20. Lotan R, Lengenova S, Rijini N & Hershkovich O. Intravenous tranexamic acid reduces blood loss in multilevel spine surgeries. *Journal of the American Academy of Orthopaedic Surgeons* 2023 **31** e226–e230. (https://doi.org/10.5435/JAAOS-D-22-00738)

21. Shi H, Zhou ZM, Xu ZY, Zhu L, Jiang ZL, Chen L & Wu XT. Risk factors for increased surgical drain output after transforaminal lumbar interbody fusion. *World Neurosurgery* 2021 **151** e1044–e1050. (https://doi.org/10.1016/j.wneu.2021.05.059)

22. Yu CC, Fidai M, Washington T, Bartol S & Graziano G. Oral is as effective as intravenous tranexamic acid at reducing blood loss in thoracolumbar spinal fusions: a prospective randomized trial. *Spine* 2022 **47** 91–98. (https://doi.org/10.1097/BRS.0000000000004157)

23. Mallepally AR, Mahajan R, Rustagi T, Goel SA, Das K & Chhabra HS. Use of topical tranexamic acid to reduce blood loss in single-level transforaminal lumbar interbody fusion. *Asian Spine Journal* 2020 **14** 593–600. (https://doi.org/10.31616/asj.2019.0134)

24. Zhang D, Wu X, Kong Q, Wang Y, Zhang B, Feng P, Wu Y, Guo C & Li W. Prospective randomized controlled trial on the effectiveness of low-dose and high-dose intravenous tranexamic acid in reducing perioperative blood loss in single-level minimally invasive transforaminal lumbar interbody fusion. *Zhongguo Xiu Fu Chong Jian Wai Ke Za Zhi* 2022 **36** 439–445. (https://doi.org/10.7507/1002-1892.202112015)

25. Hui S, Peng Y, Tao L, Wang S, Yang Y, Du Y, Zhang J, Zhuang Q & TARGETS Study Group. Tranexamic acid given into wound reduces postoperative drainage, blood loss, and hospital stay in spinal surgeries: a meta-analysis. *Journal of Orthopaedic Surgery and Research* 2021 **16** 401. (https://doi.org/10.1186/s13018-021-02548-6)

26. Yuan QM, Zhao ZH & Xu BS. Efficacy and safety of tranexamic acid in reducing blood loss in scoliosis surgery: a systematic review and meta-analysis. *European Spine Journal* 2017 **26** 131–139. (https://doi.org/10.1007/s00586-016-4899-0)

27. Honda A, Iizuka Y, Michihata N, Uda K, Mieda T, Takasawa E, Ishiwata S, Kakuta Y, Tomomatsu Y, Ito S, ***et al.*** Effect of intraoperative tranexamic acid on perioperative major hemorrhage requiring transfusion in patients undergoing elective spine surgery: a propensity score-matched analysis using a national inpatient database. *Global Spine Journal* 2022 21925682221123317. (https://doi.org/10.1177/21925682221123317)

28. Abdou M, Kwon JW, Kim HJ, Lee B, Choi YS, Moon SH & Lee BH. Tranexamic acid and intraoperative and postoperative accumulative bleeding in elective degenerative spine surgery. *Yonsei Medical Journal* 2022 **63** 927–932. (https://doi.org/10.3349/ymj.2022.0163)

29. Chauncey JM & Wieters JS. *Tranexamic Acid. Copyright © 2023*. Treasure Island, FL: StatPearls Publishing LLC 2023.

30. Foreman PM, Chua M, Harrigan MR, Fisher WS, 3rd, Tubbs RS, Shoja MM & Griessenauer CJ. Antifibrinolytic therapy in aneurysmal subarachnoid hemorrhage increases the risk for deep venous thrombosis: a case-control study. *Clinical Neurology and Neurosurgery* 2015 **139** 66–69. (https://doi.org/10.1016/j.clineuro.2015.09.005)

31. Luo H, Shen C, Qu T, Chen L, Sun Y & Ren Y. Tranexamic acid-induced focal convulsions after spinal surgery: a rare case report and literature review on side effects of accidental spinal administration of tranexamic acid. *EFORT Open Reviews* 2023 **8** 482–488. (https://doi.org/10.1530/EOR-23-0016)